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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,218	08/18/2000	Olga Yurieva	600-1-179N CON	6461
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MICHAEL L GOLDMAN NIXON PEABODY LLP CLINTON SQUARE P O BOX 31051 ROCHESTER, NY 14603-1051		EXAMINER HUTSON, RICHARD G		
		ART UNIT PAPER NUMBER		
		1652		
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		11/29/2007 PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/642,218

Applicant(s)

YURIEVA ET AL.

Examiner

Richard G. Hutson

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 8/31/2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7,22,28,29,81,83-86,88,89 and 91-98 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 91-98 is/are allowed.
- 6) ☒ Claim(s) 7,22,28,29,81,83-86,88 and 89 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's amendment of claim 7, in the paper of 8/31/2007, is acknowledged. Claims 7, 22, 28, 29, 81, 83-86, 88, 89 and 91-98 are still at issue and are present for examination. Applicants' arguments filed on 8/31/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 22, 28, 29, 81, 83-86, 88 and 89 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 7, 22, 28, 29, 81, 83-86, 88 and 89. In response to this rejection applicants have amended claim 7 and traverse the rejection as it applies to the newly amended claims.

Applicants submit that it appears the only issue is whether an adequate structure-to-function has been demonstrated for the claimed dnaX polynucleotides, which encode gamma/tau subunits and the PTO has taken the position that the data presented is inadequate to establish this relationship, specifically with respect to function. Applicants submit that the invention as claimed must be taken in the context of the prior art teachings concerning dnaX of *E. coli* and its function in encoding both tau and gamma subunits through a similar frameshift mechanism as reported in the present application. Applicants submit that the function and activity of the tau and gamma proteins of the *E. coli* Pol III holoenzyme (encoded by *E. coli* dnaX) are generally described at pages 2-4 of the present application.

Applicants submit that given the structural and functional activities shared between dnaX of *Thermus thermophilus* and the dnaX of *E. coli*, it would be reasonable for the person of skill in the art to expect the encoded gamma and tau subunits of *Thermus* species to share functions within the Pol III holoenzyme that are described at pages 2-4 of the present application (see also, Bullard et al., "DNA Polymerase III Holoenzyme from *Thermus thermophilus* Identification, Expression, Purification of Components, and Use to Reconstitute a Processive Replicase," *J. Biol. Chem.*, 277(16): 13401-13408 (2002). Thus applicants submit that one of ordinary skill in the art would have understood that applicants were in possession of the presently claimed invention at the time the application was filed.

Applicant's amendment and complete argument are acknowledged and have been carefully considered, however, have been found to be non-persuasive in

overcoming the instant rejection based upon a lack of written description. While applicants continue to argue that the presently disclosed polynucleotides share similar structure and thus function based upon this "similar structure", this conclusion remains in question. Applicant's claims continue to be drawn to those nucleic acids encoding tau and gamma subunits of a DNA polymerase III-type enzyme and these "functions" in combination with the structural limitations of the claims are insufficient to meet the requirement for the written description of the claimed genus. Applicants have now amended the claims such that the encoded Tau subunit possesses DNA stimulated ATPase activity. This functional description of the encoded Tau subunit is noted as is the lack of any functional characterization/limitation of the gamma subunit. It remains that applicants have not adequately described a structure-to-function relationship of the claimed genus of polynucleotides given the "function" of the claimed nucleic acids.

The general description of function and activity of the tau and gamma proteins of the *E. coli* Pol III holoenzyme in the present application is insufficient to describe the claimed genus.

Applicant is referred to the guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 7, 22, 28, 29, 81, 83-86, 88 and 89 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polynucleotide encoding a τ or γ subunit of a DNA polymerase III-type enzyme, wherein

said τ or γ subunit has the amino acid residue sequence represented by the formula shown in SEQ ID NO: 2 or SEQ ID NO: 4, does not reasonably provide enablement for any polynucleotide encoding a τ or γ subunit of a DNA polymerase III-type enzyme of a thermophilic bacterium, wherein said polynucleotide is a mere 90% identical to the nucleotide sequence of SEQ ID NO: 3 and said subunit comprises a GXXGXGKT ATP-binding motif. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 7, 22, 28, 29, 81, 83-86, 88 and 89. In response to this rejection applicants have amended claim 7 and traverse the rejection as it applies to the newly amended claims.

Applicants submit that the PTO continues to reject the claimed subject matter even though applicants have demonstrated, by way of a sequence comparison to members outside the claimed genus (see Figure 5), those regions of the tau (and gamma) proteins that are highly conserved among distantly related homologs. Applicants submit that this certainly would allow the skilled scientist to understand generally those regions that would not tolerate much variation in structure while still retaining tau/gamma function, i.e., highly conserved regions would tolerate less variance. Applicants submit that thus, it is improper to conclude that applicants have not demonstrated "which of the essentially infinite possible choices is likely to be successful."

Applicants submit that for these reasons, it is apparent that the present application fully enables the presently claimed invention. Therefore, the rejection under 35 U.S.C. § 112 (1st para.) for lack of enablement is improper and should be withdrawn.

Applicant's amendment and complete argument has been considered, however, continues to not be found persuasive for the reasons previously stated and repeated below.

Applicants submission of the sequence comparisons showing regions conserved between distantly related homologs, while presenting some guidance as to the relationship between these "distantly related homologs", is insufficient to enable the presently claimed genus of polynucleotides drawn to any polynucleotide encoding a γ subunit or a τ subunit of a DNA polymerase III-type enzyme having a mere 90% identity to the nucleotide sequence of SEQ ID NO: 3.

It continues that while methods to produce variants of a known sequence are well known to the skilled artisan, producing the genus of variants as claimed by applicants (i.e., encoding a DNA polymerase type-III τ or γ subunit) requires that one of ordinary skill in the art know or be provided with sufficient guidance for the selection of which of the larger number of variants have the desired properties. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the

experimentation should proceed. Applicants sequence comparisons are acknowledged but found insufficient to enable the breadth of the claimed genus. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting τ or γ subunit activity; (B) the general tolerance of τ or γ subunits to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a DNA polymerase III enzyme τ or γ subunit with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the delta subunit activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those DNA molecules of the claimed genus which encode a polypeptide with DNA polymerase III enzyme τ or γ subunit activity.

It continues that applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including the claimed DNA molecules encoding a DNA polymerase III-type enzyme τ or γ subunit. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those polynucleotides having the desired biological characteristics is unpredictable and the

experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

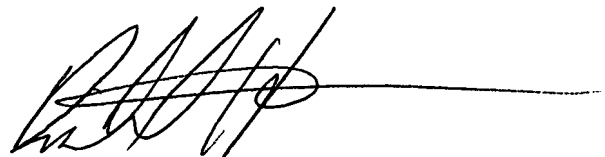
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax

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phone number for the organization where this application or proceeding is assigned is
703-872-9306.

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you have questions on access to the Private PAIR system, contact the Electronic
Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'R. G. Hutson', followed by a long horizontal line extending to the right.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rg
11/20/2007